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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,773	01/26/2004	Hrair Kirakossian	138.00US	2462

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/765,773	KIRAKOSSIAN ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4-8,11,12 and 17-20* is/are allowed.

6)☒ Claim(s) *1-3, 9-10, 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry & Claim Status

The amendment filed on February 21, 2006 has been acknowledged and entered.

Claims 1-8 and new claims 9-20 are pending.

Withdrawn Rejection(s)

Rejections under 112, 1st and 2nd paragraphs are withdrawn herein.

Maintained Rejection(s)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9, 10, 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terstappen et al. (US 6,365,362) in view of Ness et al. (US 6,815,212).

Terstappen teaches a method of magnetically isolating a rare cell type from a mixed population of cells, the method comprises the steps of: mixing colloid magnetic particles conjugated with a monoclonal antibody reactive with the rare cell determinant or a class of determinants different than those found on blood cells with a population of

cells containing a rare cell type; applying a magnetic field to isolated the bound complex from the unbound magnetic particles-antibody conjugates; Adding a second set of monoclonal antibodies (binding compound), labeled with reporter molecules (tag) to the isolated portion of the sample containing the rare cell type; separating the cells from the unbound by using a magnetic field; detecting the bound portion by microscopy, flow cytometry, or other analytical platforms such as bright field base image analysis, capillary volumetry, spectral imaging analysis, automated cell analysis. (see col. 8, lines 29-53). Detectable labels are detected based on light absorbance, fluorescence, reflectance, light scatter, phosphorescence, luminescence properties etc. (see col. 13, lines 45-50). Biospecific reagents are antibodies having specificity for an epitope (biomarkers) which differs from that used to immunomagnetically select the cells. (see col. 16, lines 1-5). Terstappen also teaches detecting kinase receptor. (see col. 10, lines 45-50). Terstappen teaches that the rare cell types are fetal cells and cancer cells. (see col. 13, lines 6-7). Terstappen teaches that the sample is a patient, biological, blood sample. (see col. 16, lines 32-33).

However, Terstappen fails to teach releasing the tags of the binding compound, separating and identifying the released tags to determine one or more biomarkers in the sample.

Ness teaches an assay method comprising of combining a set of first tagged members with a biological sample containing a second member of a ligand pair to permit binding or formation of a complex between the first and second members; the second member may be attached to a solid phase such as magnetic particles (see col.

4, line 9); separating the bound first and second members from unbound members; cleaving the tag from the tagged first member and detecting the tag by spectroscopic such as mass spectrometers or potentiometric methods (see col. 14, line 65-col. 15, line 5). Mass spectrometers use the difference in the mass-to charge ratio of ionized atoms or molecules to separate them from each other. Mass spectrometry is therefore useful for quantitation of atoms or molecules and also for determining chemical and structural information about molecules. Molecules have distinctive fragmentation patterns that provide structural information to identify compounds. (see col. 62, lines 57-64). Detection is carried out using fluorescence tag and detecting their absorption, emission, etc. 9see col. 18,lines 43-65). A wide variety of first and second member pairs are used including nucleic acids, proteins, polypeptides (antibodies or antibody fragments – monoclonal or polyclonal or binding partners as a CDR- complementary determine region-), antibody/protein, antibody/antigen (see col. 40, lines 40-55). Samples are isolated and purified cell types (see col. 47, lines 24-25).

It would have been obvious to one of ordinary skills in the art to use cleave the tag and analyze the tags as taught by Ness as a detection step to detect biomarkers of cells isolated according to the method of Terstappen and would have a reasonable expectation of success because both references teach using magnetic particles as solid phase and detection based on light absorbance, fluorescence, reflectance, light scatter, etc. and both methods are applicable to cell samples. The advantage of cleaving a tag after separation of bound and unbound is an enhanced sensitive detection method

because the tag alone reduces non-specific background which might be produced if the target was bound to the tag.

Claims 2-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terstappen and Ness as applied to claim 1 above, and further in view of Wels et al. (US 5,571,894).

Terstappen and Ness have been discussed above.

However, both Terstappen and Ness fail to teach the capture antigen is a receptor tyrosine kinase such as an ErbB receptor.

Wels discusses that growth factors and their receptors are involved in the regulations of cell proliferation and they also play a role in tumor growth. Thus, c-erbB-2 growth factor receptor protein, a protein of the membrane receptor protein tyrosine kinase family is found in human breast tumors and human ovarian carcinomas. Thus, the c-erbB 2 protein has potential, both as a diagnostic marker and as a target for cancer therapy. (see col. 10-25).

Since Terstappen teaches using a kinase receptor as a receptor on cell for detecting cancer cells and Ness teaches a method of detecting cancerous cells, it would have been obvious to one of ordinary skills in the art to use antibodies that bind to erbB receptor of the tyrosine kinase receptor family as taught in Wels to detect cancer cells according to the combined method of Terstappen and Ness because cancer cells have erbB or tyrosine kinase receptor on their membrane.

Response to Arguments

Applicant's arguments filed February 21, 2006 have been fully considered but they are not persuasive.

Regarding the 103 rejection, Applicants argue that since Terstappen discloses a highly sensitive assay to detect, enumerate and characterize carcinoma cells in the blood, one skilled in the art would have no motivation to combine the cleavable tags of Ness with immunomagnetic separation methods of Terstappen into a single biomarker detection assay.

Biomarkers are known in the art to be a hormone, a nucleic acid, or a peptide. Thus, in detecting a nucleic acid, using cleavable tags has many advantages, such as the ability to collect tags for a specified period of time prior to measurement, the ability to detect DNA with lengths greater than 450 nucleotides, and the use of cleavable tags in sequencing has the additional advantage of allowing the user to employ the most efficient and sensitive DNA separation method which also possesses the highest resolution. Thus, one skilled in the art would be motivated to combine the cleavable tags of Ness with the immunomagnetic separation of Terstappen into a single biomarker detection assay.

No further discussion on the 103 rejection of claim 2 is necessary since it has been explained above of the motivation to combine Terstappen in combination with Ness.

Claims 3 was intended to be rejected along with claim 2 in the previous office action because the rejection discussed an ErbB receptor.

Newly added claims 9-10, 13-16 are now rejected under 103 by Terstappen in view of Ness along with claim 1.

Allowable Subject Matter

Claims 4-8, 11-12, 17-20 are allowed.

The prior arts fail to teach a method of detecting a protein-protein complexes of a rare cell type in a sample containing a mixed population of cells such that each protein-protein complex has a first protein and a second protein, the method comprises the steps of immunomagnetically isolating from the sample a subpopulation of cells containing a rare cell type by contacting the sample with one or more antibody compositions, each antibody composition being specific for a capture antigen and being attached to a magnetic particle; providing a first binding compound conjugated with a cleavable tag; such first binding compound is specific for the first protein; and a second binding compound conjugated to a cleaving inducing moiety; such second compound is specific for the second protein; combining the subpopulation, the first binding compound; the second binding compound so that the tag is cleaved; separating and identifying the released tags to determine the protein-protein complex in the sample.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
September 1, 2006

LONG V. LE 09/05/06
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